

## THE CLAIMS

Please amend and/or cancel the claim(s) of the captioned application, and/or add claim(s) to the captioned application, in accordance with the following annotations and/or mark-ups showing all change(s) relative to the previous version(s) of the claim(s) as required by 37 C.F.R. 1.121:

Claim 1 (Currently amended). A method for producing an index indicative of brain disease comprising the steps of:

collecting positron emission tomographic image data showing metabolic activity in the brain of a patient;

spatially normalizing ~~said~~ the image data using a standardized three dimensional coordinate system;

spatially filtering the normalized image data;

utilizing statistical mapping procedures to create a plurality of three-dimensional volumes of interest;

selecting specific ~~regions of the brain~~ volumes of interest showing extremes in metabolic activity;

collecting mean intensity values for the normalized, filtered image data from ~~said the~~ selected ~~specific brain regions~~ volumes of interest;

weighting ~~said the~~ mean intensity values with standard weights derived from the group analysis used to create the standard; and

normalizing the ratio of ~~said the~~ mean, weighted, metabolic activity image data to produce a numerical index.

Claim 2 (Previously presented). The method according to claim 1 wherein the metabolic activity is indicated by glucose metabolism of brain cells.

Claim 3 (Previously presented). The method according to claim 1 wherein the three-dimensional coordinate system is Talairach space.

Claim 4 (Previously presented). The method according to claim 3 wherein the image data is transformed to conform in Talairach space using a twelve parameter, linear, affine algorithm.

Claim 5 (Previously presented). The method according to claim 1 wherein the transformed image data is filtered using an eight millimeter, isotropic, Gaussian filter kernel.

Claim 6 (Currently amended). The method according to claim 1 wherein ~~said~~ the normalized, filtered image data is compared to data from age-matched patient controls using Standard Parametric Mapping techniques in a statistical group comparison.

Claim 7 (Previously presented). The method according to claim 6 wherein the Standard Parametric Mapping is used to generate a map of the brain and the map is converted to a unit normal distribution Z score.

Claim 8 (Previously presented). The method according to claim 7 wherein the Standard Parametric Mapping Z-score results are utilized to select specific regions of the brain showing extremes in metabolic activity.

Claim 9 (Canceled).

Claim 10 (Currently amended). The method according to claim [9] 1 wherein mean intensity values for the volume elements are contained within each of ~~said~~ the volumes of interest are determined wherein each ~~said~~ volume element is a cube of selected dimension.

Claim 11 (Currently amended). The method according to claim [9] 1 wherein each of a plurality of volumes of interest is placed at specific coordinates in ~~said~~ the three dimensional coordinate system.

Claim 12 (Currently amended). The method according to claim [9] 1 wherein two sets of volumes of interest are selected, the first set being comprised of a plurality of volumes of interest with increased metabolism and the second set being comprised of a plurality of volumes of interest with decreased metabolism.

Claim 13 (Canceled).

Claim 14 (Currently amended). The method according to claim 13 wherein ~~said~~ the volumes of interest with increased metabolism comprise the vermis, motor, R pons and cerebellar nuclei and ~~where said~~ wherein the volumes of interest with decreased metabolism comprise the posterior cingulate, L parietal, R parietal01 temporal01, and temporal02.

Claim 15 (Currently amended). The method according to claim 12 additionally comprising:

normalizing the intensity data of ~~said~~ the volumes of interest, ~~said~~ the mean normalization comprising dividing each intensity value from each volume

of interest by the average of the values of ~~said~~ the intensities, thereby establishing a mean value of one (1) for each subject's data set;

dividing the data sets into evenly valued subgroups with designation of  $c_i$  for the  $i^{\text{th}}$  control subgroup and  $p_i$  for the  $i^{\text{th}}$  patient subgroup;

forming mixed groups by pairing controls with patients to yield small data sets for use in training an artificial neural network;

rescaling ~~said~~ the small data sets to appropriately match the input range of ~~said~~ the data sets to the range of an output transfer function;

utilizing ~~said~~ the rescaled output from ~~said~~ the transfer function as inputs for training an artificial neural network to produce the neural network cognitive decline index (CDInn); and

testing ~~said~~ the CDInn on the full data set to assess the classification accuracy of ~~said~~ the CDInn.

Claim 16 (Currently amended). The method according to claim 15 wherein ~~said~~ the output transfer function comprises a linear function.

Claim 17 (Currently amended). The method according to claim 15 additionally comprising utilizing the outputs from ~~said~~ the transfer function as inputs for a second output transfer function.

Claim 18 (Currently amended). The method according to claim 15 wherein ~~said~~ the output transfer function comprises a linear function and ~~said~~ the second output transfer function comprises a tangent sigmoidal transfer function.

Claim 19 (Canceled).

Claim 20 (Currently amended). The method according to claim 12 wherein the intensity values of ~~said~~ the volumes of interest are used to create a first and second data set, ~~said~~ the first data set comprising the ratios of the mean value of the intensities of the first set of volumes of interest with increased metabolism divided by the intensity values of each of the volumes of the second set of volumes of interest with decreased metabolism and ~~said~~ the second data set comprising the ratios of each of the intensity values of the first set of volumes of interest with increased metabolism divided by the mean value of the intensities of the second set of volumes of interest with decreased metabolism.

Claim 21 (Currently amended). The method according to claim 15 wherein the intensity values of the set of ~~said thirteen~~ volumes of interest are used to create a third

and fourth data set, ~~said~~ the third data set comprising the ratios of the mean of the intensity value of the set of ~~four~~ volumes of interest with increased metabolism divided by the intensity values of each of the ~~nine~~ volumes of interest with decreased metabolic activity and the fourth data set comprising the ratio of each of the intensity values of the set of ~~four~~ volumes of interest of increased metabolic activity divided by the mean value of the intensities of the volumes of interest with increased metabolic activity.

Claim 22 (Canceled).

Claim 23 (Currently amended). The method according to claim 1 additionally comprising:

using ~~said~~ the weighted intensity values as a baseline reference for iterative optimization of each weighted intensity value;

forming a subset of weights taken from a control subject database, the ~~said~~ control subjects forming a first group;

maximally separating each of ~~said~~ the weighted intensity values of each region taken from ~~said~~ a patient from intensity values of analogous regions taken from the control subjects using a dynamic table of patient weights and control subject weights wherein separations in intensity values between the patients and the normal controls are assessable in real time;

merging patient data with data from previous patients in a patient database to constitute a second group;

iteratively adjusting ~~said~~ the weighted intensity values to maximize the separation between ~~said~~ the patient and ~~said~~ the control subjects while minimizing within-group variance; and

calculating a second Cognitive Decline Index utilizing the optimized weighted intensity values.

Claim 24 (Canceled).

Claim 25. (Presently amended) Apparatus for producing an index indicative of brain pathology resulting from injury, disease, or other cause ~~comprising:~~

~~a positron emission tomographic scanner; and~~

~~a computer operatively connected to the outputs of said PET scanner, said computer being programmed to calculate an index indicative of brain disease by:~~

~~collecting positron emission tomographic image data showing  
metabolic activity in the brain of a patient;  
spatially normalizing said image data using a standardized three  
dimensional coordinate system;  
spatially filtering the normalized image data;  
selecting specific regions of the brain showing extremes in  
metabolic activity;  
collecting mean intensity values for the normalized, filtered  
image data from said selected specific brain regions;  
weighting said mean intensity values with standard weights  
derived from the group analysis used to create the standard; and  
normalizing the ratio of said mean, weighted, metabolic activity  
image data to produce a numerical index by the method of claim 1.~~

Claims 26-46 (Canceled).